

Status of the Claims and Listing of Claims:

In the Advisory Action mailed August 1, 2005, the Examiner stated that the claim amendments presented in the amendment filed June 24, 2005 would be entered in the case. The listing of claims set forth below reflects the status of the claims following entry of the June 24, 2005 amendments, and are presented for the convenience of the Examiner.

Claims 1. - 104. (Canceled).

105. (Previously presented) A method of treating recurrent miscarriage by inducing immune tolerance to a paternal antigen in a mammalian prospective mother lacking said immune tolerance, said method comprising exposing a mucosal surface of said prospective mother to:

a) semen or an MHC Class I antigen of a prospective father capable of eliciting a Th-1 response; and

b) a substantially purified TGF β selected from the group consisting of TGF β 1, TGF β 2, and TGF β 3,

wherein the exposure is at a time and in an amount effective to induce said immune tolerance and is at least one week before attempted conception.

106. (Currently Amended) The method according to ~~any one of claims 105, 141, 142, 143, or 144~~ **claim 105 or 141**, wherein the prospective mother and father are both human.

107. (Currently Amended) The method according to ~~any one of claims 105, 141, 142, 143, or 144~~ **claim 105 or 141**, wherein the TGF β and the semen or MHC Class I antigens are administered at one site.

108. (Currently Amended) The method according to ~~any one of claims 105, 141, 142, 143, or 144~~ **claim 105 or 141**, wherein the TGF β and the semen or MHC Class I antigen are respectively administered at a first site and a different site.

109. (Currently Amended) The method according to ~~any one of claims 105, 141, 142, 143, or 144~~ **claim 105 or 141**, wherein the TGF β and the semen or MHC Class I antigen are administered temporally spaced apart.

110. (Previously Presented) The method according to claim 109, wherein the semen or MHC Class I antigen is administered subsequent to an administration of TGF β .

111. (Previously Presented) The method according to claim 109, wherein the semen or MHC Class I antigen is administered first followed by administration of TGF β .

112. (Currently Amended) The method according to ~~any one of claims 105, 141, 142, 143, or 144~~ **claim 105 or 141**, wherein the MHC Class I antigen is from sperm cells of the prospective father.

113. (Currently Amended) The method according to ~~any one of claims 105, 141, 142, 143, or 144~~ **claim 105 or 141**, wherein the semen or MHC Class I antigen is presented in purified or semi-purified form.

114. (Previously Presented) The method according to claim 113, wherein the purified or semi-purified semen or MHC Class I antigen is presented on an inert or adjuvant carrier.

115. (Canceled).

116. (Currently Amended) The method according to ~~any one of claims 105, 141, 142, 143, or 144~~ **claim 105 or 141**, wherein the TGF β is supplied in a slow release form.

117. (Currently Amended) The method according to ~~any one of claims 105, 141, 142, 143, or 144~~ **claim 105 or 141**, wherein the exposure of the semen or MHC Class I antigen is to the prospective mother's genital tract in the form of the prospective father's ejaculate.

118. (Currently Amended) The method according to ~~any one of claims 105, 141, 142, 143, or 144~~ **claim 105 or 141**, wherein the mucosal surface is selected from the group comprising of an oral mucosal surface, a respiratory mucosal surface, a gastrointestinal mucosal surface and a genital mucosal surface.

119. (Currently Amended) The method according to ~~any one of claims 105, 141, 142, 143, or 144~~ **claim 105 or 141**, wherein the mucosal surface is a genital mucosal surface.

120. (Canceled).

121. (Currently Amended) The method according to ~~any one of claims 105, 141, 142, 143, or 144~~ **claim 105 or 141**, wherein the mucosal surface is exposed to a concentration of TGF β of 100ng/ml.

122. (Currently Amended) The method according to ~~any one of claims 105, 141, 142, 143, or 144~~ **claim 105 or 141**, wherein the mucosal surface is exposed to a concentration of TGF β of 200ng/ml.

123. (Canceled).

124. (Currently Amended) The method according to ~~any one of claims 105, 141, 142, 143, or 144~~ **claim 105 or 141**, wherein TGF β is administered in its active form.

125. (Currently Amended) The method according to ~~any one of claims 105, 141, 142, 143, or 144~~ **claim 105 or 141**, wherein the prospective mother is incapable of converting a sufficient amount of the inactive form of TGF β to active TGF β , and the method includes administration of active TGF β .

126. (Currently Amended) The method according to ~~any one of claims 105, 141, 142, 143, or 144~~ **claim 105 or 141**, wherein the prospective mother is incapable of converting the

inactive form of TGF β to active TGF β , and the method includes administration of plasmin, so as to increase the level of active TGF β .

127. (Currently Amended) The method according to ~~any one of claims 105, 141, 142, 143, or 144~~ **claim 105 or 141**, wherein the prospective mother and father are human and the exposure to TGF β and the semen or MHC Class I antigen of the prospective father is a multiple exposure.

128. - 131. (Canceled).

132. (Currently Amended) The method according to ~~any one of claims 105, 141, 142, 143, or 144~~ **claim 105 or 141**, wherein administration of TGF β and the semen or MHC Class I antigen occurs at least once after attempted conception.

133. (Currently Amended) The method according to ~~any one of claims 105, 141, 142, 143, or 144~~ **claim 105 or 141**, further including a step, prior to exposure to antigen and TGF β , of diagnosing or testing whether

- (a) the prospective father has adequate levels of TGF β ;
- (b) the prospective mother has the capacity to activate TGF β , or
- (c) anti-sperm antibodies are present in the prospective mother.

134. (Currently Amended) The method according to ~~any one of claims 105, 141, 142, 143, or 144~~ **claim 105 or 141**, used in conjunction with IVF treatment.

135. - 140. (Canceled).

141. (Previously Presented) A method of treating recurrent miscarriage by inducing immune tolerance to a paternal antigen in a mammalian prospective mother lacking said immune tolerance, said method comprising exposing a mucosal surface of said prospective mother to:

- a) semen or an MHC Class I antigen of a prospective father capable of eliciting a Th-1 response; and

b) a substantially purified TGF β selected from the group consisting of TGF β 1, TGF β 2, and TGF β 3,

wherein the exposure is at a time and in an amount effective to induce said immune tolerance and is performed over a period spanning at least three months prior to attempted conception.

142. (Currently amended) **The method according to claim 105 or 141** ~~A method of treating recurrent miscarriage by inducing immune tolerance to a paternal antigen in a mammalian prospective mother lacking said immune tolerance, said method comprising exposing a mucosal surface of said prospective mother to:~~

~~a) semen or an MHC Class I antigen of a prospective father capable of eliciting a Th-1 response; and~~

~~b) a substantially purified TGF β selected from the group consisting of TGF β 1, TGF β 2, and TGF β 3,~~

~~wherein the exposure is at a time and in an amount effective to induce said immune tolerance and continues over a period of the first 12 weeks of pregnancy~~

143. (Currently amended) **The method according to claim 105 or 141** ~~A method of treating recurrent miscarriage by inducing immune tolerance to a paternal antigen in a mammalian prospective mother lacking said immune tolerance, said method comprising exposing a mucosal surface of said prospective mother to:~~

~~a) semen or an MHC Class I antigen of a prospective father capable of eliciting a Th-1 response; and~~

~~b) a substantially purified TGF β selected from the group consisting of TGF β 1, TGF β 2, and TGF β 3,~~

~~wherein the exposure is at a time and in an amount effective to induce said immune tolerance and the mucosal surface is exposed to a concentration of TGF β of between 100 and 400 ng/ml.~~

144. (Currently amended) **The method according to claim 105 or 141** ~~A method of treating recurrent miscarriage by inducing immune tolerance to a paternal antigen in a mammalian prospective mother lacking said immune tolerance, said method comprising exposing a mucosal surface of said prospective mother to:~~

~~a) semen or an MHC Class I antigen of a prospective father capable of eliciting a Th-1 response; and~~

~~b) a substantially purified TGF β selected from the group consisting of TGF β 1, TGF β 2, and TGF β 3,~~

~~wherein the exposure is at a time and in an amount effective to induce said immune tolerance and the mucosal surface is exposed to a concentration of TGF β of between 100 and 400 ng/mL, with a total dose of between 100 to 2000 ng.~~